Abstract

Introduction

Cancer is one of the main problems worldwide and is the second leading cause of death after cardiovascular diseases. Cancer is the due to a series of molecular events that by inactivating of cell proliferation control systems, lead to excessive cell growth and division and attacks other tissues. Cancer is mainly treated by three methods, surgery, radiation therapy and systemic treatment. Despite advances in cancer prevention and treatment, problems such as resistance to existing drugs and severe side effects of drugs due to their low selectivity require researchers to design and develop new structures with more potency.

Materials and Methods

According to studies on the cytotoxicity of some compounds, in this project a series of new 1,2,3,4-tetrahydropyrimidine derivatives were synthesized using the Biginelli reaction and after purification, structures of the synthesized compounds were confirmed by ^{1}H-NMR, FT-IR and MS spectra. Thus, the cytotoxicity of the synthesized compounds evaluated against three A549, Hep-G2 and MCF-7 human cancer cell lines using MTT assay.

Results

Our results showed, compound benzyl 6-methyl-4- (4-nitro phenyl) -2-thioxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (S8) having the electron withdrawing group (NO_2) at *para* position of phenyl ring on C4 position, thioxo group at C2 and benzyl carboxylate group at C5 was the most potent compound among all compounds against three cell lines (IC_{50} = 65.54 µM in MCF-7 cell line, IC50 = 73.71µM in Hep-G2 cell line and IC50 = 43.97 µM in A549). According to the results of the statistical analysis, the cytotoxic effect of all the derivatives synthesized at all concentrations was significantly different compared to the negative control group ($P< 0.05$) and all concentrations of the synthesized compounds had significant inhibitory effects in all three periods of 24, 48 and 72 hours compared to similar concentrations of doxorubicin as positive control ($P<0.05$). Also, the viability of cells treated with four concentrations of synthetic compounds in cancer cells ($P<0.05$) and normal cells at all concentrations was significantly different and at 100 µM concentration more significant for most compounds ($P< 0.01$). The cytotoxicity results of these compounds on Human umbilical vein endothelial cell (HUVEC) as normal cell line also showed that they were partially selective. Among compounds, compound S1 was more selective against three cell lines at the 100 µM concentration.

Discussion and conclusion

Investigation of the structure-activity relationship of the synthesized compounds indicates that the increase lipophilicity and the presence of strong electron withdrawing group at the C4 position of phenyl ring increases cytotoxicity.

Keywords: Cancer, 1,2,3,4-Tetrahydro pyrimidine, Cytotoxicity